1: J Biol Chem. 1995 Apr 7;270(14):7795-8.

A novel protein that interacts with the death domain of Fas/APC contains a sequence motif related to the death domain.

Boldin MP, Varfolomeev EE, Pancer Z, Mett IL, Camonis JH, Wallach I

Department of Membrane Research and Biophysics, Weizmann Institute of Science, Rehovot, Israel.

Signaling for cell death by Fas/APO1 occurs via a distinct region in its intracellular domain. This region contains a conserved sequence motif, the death domain motif, that is also found in the intracellular domains of the p55 tumor necrosis factor receptor and the low affinity nerve growth factor receptor, as well as in the regulatory domain of the ankyrins. A novel protein that specifically binds to the death domain of Fas/APO1 but not to Fas/APO1 molecules with a loss of function point mutation occurring in lprcg mice was cloned by a two-hybrid screen of a HeLa cells' cDNA library. The cloned protein itself contains a death domain motif, and this region binds to the deat domain of Fas/APO1, while the region upstream to the death domain prompt self-association of the protein. Induced expression of the protein results in ligand-independent triggering of cytotoxicity, suggesting that it is involved ir cell death induction by Fas/APO1.

PMID: 7536190 [PubMed - indexed for MEDLINE]

1: Cell. 1996 Jun 14;85(6):803-15.

Involvement of MACH, a novel MORT1/FADD-interacting protease, in Fas/APO-1- and TNF receptor-induced cell death.

Boldin MP, Goncharov TM, Goltsev YV, Wallach D.

Department of Membrane Research and Biophysics, The Weizmann Institute Science, Rehovot, Israel.

Fas/APO-1 and p55 tumor necrosis factor (TNF) receptor (p55-R) activate cellular mechanisms that result in cell death. Upon activation of these recept Fas/APO-1 binds a protein called MORT1 (or FADD) and p55-R binds a protein called TRADD. MORT1 and TRADD can also bind to each other. W have cloned a novel protein, MACH, that binds to MORT1. This protein exis in multiple isoforms, some of which contain a region that has proteolytic activity and shows marked sequence homology to proteases of the ICE/CED family. Cellular expression of the proteolytic MACH isoforms results in cell death. Expression of MACH isoforms that contain an incomplete ICE/CED- region provides effective protection against the cytotoxicity induced by Fas/APO-1 or p55-R triggering. These findings suggest that MACH is the m upstream enzymatic component in the Fas/APO-1- and p55-R-induced cell death signaling cascades.

PMID: 8681376 [PubMed - indexed for MEDLINE]

1: Science. 1998 Mar 20;279(5358):1954-8. Related Articles, Li

Full text article at www.sciencemag.org

FADD: essential for embryo development and signaling from some, but not all, inducers of apoptosis.

Yeh WC, Pompa JL, McCurrach ME, Shu HB, Elia AJ, Shahinian A, N M, Wakeham A, Khoo W, Mitchell K, El-Deiry WS, Lowe SW, Goeddel DV, Mak TW.

Amgen Institute, University of Toronto, Toronto, Ontario, Canada.

FADD (also known as Mort-1) is a signal transducer downstream of cell deat receptor CD95 (also called Fas). CD95, tumor necrosis factor receptor type 1 (TNFR-1), and death receptor 3 (DR3) did not induce apoptosis in FADD-deficient embryonic fibroblasts, whereas DR4, oncogenes E1A and c-myc, a chemotherapeutic agent adriamycin did. Mice with a deletion in the FADD gene did not survive beyond day 11.5 of embryogenesis; these mice showed signs of cardiac failure and abdominal hemorrhage. Chimeric embryos showi a high contribution of FADD null mutant cells to the heart reproduce the phenotype of FADD-deficient mutants. Thus, not only death receptors, but al receptors that couple to developmental programs, may use FADD for signali

PMID: 9506948 [PubMed - indexed for MEDLINE]